

AAU

TASK FORCE ON RESEARCH ACCOUNTABILITY	REPORT AND RECOMMENDATIONS
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Report on University Protections of Human Beings Who Are the Subjects of Research

ASSOCIATION OF AMERICAN UNIVERSITIES

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ASSOCIATION OF AMERICAN UNIVERSITIES	
<i>Task Force on Research Accountability</i>	INTRODUCTION

The Association of American Universities believes it is vital for leaders of the academic community to ensure that research conducted on our campuses meets the highest ethical standards and promotes the public health. AAU therefore established the Task Force on Research Accountability in March, 2000. The Task Force's first assignment was to assess university research management challenges related to the protection of human subjects;

its second will be to examine issues that arise from the increasing collaboration between industry and our research universities. In both areas, the Task Force is charged with developing recommendations for providing appropriate accountability and oversight of university research and regulatory compliance. This is the report on human subjects research.

BACKGROUND

A crucial part of the recent dramatic advances in prevention and treatment of diseases has been research involving the informed and voluntary participation of human subjects. Federal policy is designed to protect human subjects while fostering continued research advances. Federal laws and regulations are based on long-standing moral principles regarding the protection of human subjects and the practice of informed consent, and they govern how federal grantees, such as research universities and their principal investigators, are to administer research and provide human subjects protections.

Federal regulations require grantees to create ethical oversight committees, known as institutional review boards (IRBs). The IRBs are responsible for reviewing and approving research involving human subjects in accordance with federal laws designed to protect the rights and welfare of human subjects. IRBs work to ensure that individuals who agree to participate in studies fully understand the nature of the research, willingly consent to participate, and are properly monitored throughout the study. Universities, through their university-wide as well as their collegiate and departmental leadership, have the responsibility to ensure that researchers adhere to these processes. The federal government uses oversight processes in the Department of Health and Human Services (HHS) to ensure that universities comply with these regulatory requirements. Specifically, the Food and Drug Administration (FDA) has oversight responsibility for all clinical trials that test new drugs, biologic products, and devices, and the National Institutes of Health (NIH) has had oversight responsibility for ensuring the safety of persons enrolled in research funded by HHS. NIH's responsibilities in this area were re-assigned to a new Office for Human

Research Protections within the HHS Secretary's office on June 18, 2000.

In recent years, numerous reports by the HHS Inspector General and the General Accounting Office (GAO), and enforcement actions taken by NIH's Office for Protection from Research Risks (OPRR), have called attention to some problems with university compliance with the human subjects regulations. These reports point out that IRBs have not always had the institutional support and resources necessary to do their jobs in a way that would meet the highest standards, and researchers and administrative staff have not always been as well trained as they should have been. Finally, the system of human subjects protections on campuses has not always been subject to the continuing review and monitoring it needs to ensure that it is functioning as well as this vital area of research protections requires.

The Task Force examined these reports, and reviewed recommendations for improvement that have been made by various parties, including the HHS Inspector General, the National Bioethics Advisory Commission, the OPRR, the NIH, the FDA, and associations of academic institutions, faculty and IRB administrators. It also canvassed the institutions of the Task Force members for practices and implementation steps that have been successful on their campuses. It then identified general principles to guide its deliberations, and developed the recommendations that are presented below. As the Task Force recommendations were being finalized, HHS Secretary Shalala announced several new initiatives to further strengthen protections of human research subjects in clinical trials, many of which are consistent with the proposals included in this Task Force report.

GUIDING PRINCIPLES

Human subjects research has long been and should continue to be anchored upon the principles of beneficence, justice, and respect for individuals. Two of the important pillars that assure implementation of these principles are informed consent and independent review of research protocols. Universities are committed to conducting research involving human subjects consistent with these principles, which have long guided research and which were enunciated in the reports of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979 and the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in 1981.

Research with humans plays an essential role in combating disease and in expanding the frontiers of knowledge, both of which are among the basic functions of research universities. Only through research can proven advances be made in preventing, diagnosing, and curing illness. However, it is imperative that this important activity be carried out without needless risk to or distress for, and with the voluntary and enlightened consent of, the persons who are the subjects of such research. Therefore, the performance of human subjects research must be viewed as a privilege, not a right.

Recently, there have been events indicating that implementation of protections for human subjects has not uniformly met the highest standards, and that improvements are necessary. Campuses therefore must take immediate steps to ensure a culture of compliance with appropriate protections for human subjects.

It must be recognized that administrators, faculty and research staff all have responsibilities to ensure the proper administration of human subjects research. These groups must work together to make necessary improvements so that research involving human subjects can best promote the search for new knowledge and the improvement of public health while providing all the appropriate protections of individual study participants.

Ensuring that the principles of beneficence, justice, and respect for individuals, and the practices of informed consent and independent protocol review are adhered to will provide increased accountability, so that the public will have complete confidence that human subjects are being treated on university campuses in a manner consistent with the highest ethical standards.

RECOMMENDATIONS

The Task Force recommendations listed below follow from the Task Force's Guiding Principles, and list the areas where campuses are urged to increase protections for human subjects.

The recommendations focus on actions that AAU institutions are urged to take. Being thus focused on university activities, they do not address such questions as extending IRB requirements to industrial sponsors or granting additional sanction authority to federal agencies. Further, they address human subjects research on campuses as a whole – including both medical research and social science research. While there are clear differences between the two, the overall human subjects rules apply campus-wide, which is the frame of reference for AAU presidents and chancellors.

The recommendations themselves are interlocking. The Task Force believes that protections for human subjects in US universities can attain the highest standards through a combination of:

1. increasing vigilance by senior university management;
2. training and examining of all staff and researchers involved in human subjects research;
3. strengthening IRB training, support, and operations;
4. increasing resource availability; and
5. ensuring public accountability by increasing information available to the public about university systems protecting human subjects.

1. Increasing Vigilance by Senior University Management

- a) Senior university management should state clearly to their entire campus communities the importance

of conducting human subjects research in accordance with the highest standards of ethical conduct, as described in the Guiding Principles.

- b) Institutions should maintain ongoing communications between senior management and IRBs.
- c) Senior management should receive regular independent, self-monitoring reports (also referred to as institutional audits) of the entire system for protecting human subjects on their campuses. This would include IRB administration, compliance with informed consent procedures approved by the IRBs, and full implementation of applicable laws, regulations, and campus requirements.
- d) The university community should request that HHS agencies (including NIH, FDA, and the Office for Human Research Protections) advise senior university management whenever they contact a principal investigator or other researchers with respect to human subjects protections.

2. Training and Examining of All Researchers and Staff Involved in Human Subjects Research

Universities must ensure that all personnel (faculty, researchers, management, administrative staff) directly involved in human subjects research understand the applicable laws, regulations, and ethical standards governing the protection of human subjects. All personnel engaged in the direct conduct of such research should be required to receive appropriate education designed for their level of involvement.¹

¹Much of this training could be web-based, and therefore available for use whenever it was most convenient to the personnel. NIH's web-based training program for intramural staff could be one basis for such training modules, as could some of the training materials in use at various member institutions.

Upon completion of training, an examination geared to each person's level of involvement should be administered, resulting in a designation (e.g., credentialing or certification) that the individual may engage in human subjects research. In addition to meeting the new training requirements instituted by the NIH which take effect on October 1, 2000, all persons engaged in human subjects research should receive such a designation within the next 12-18 months. After such time, universities should not submit grant applications or funding proposals to research sponsors without ensuring that the appropriate personnel have received such a designation.

Campuses would also be expected to remove such designations from any personnel found to be out of compliance with human subjects protections.

3. Strengthening IRB Training, Support, and Operations

- a) IRB members and staff must receive sufficient training to carry out their responsibilities, both initially upon joining the IRB or its staff and periodically thereafter. This would include training on all extant rules and regulations regarding human subjects research.
- b) IRB members should receive the time necessary to fulfill the functions of the Board and receive appropriate recognition and support.
- c) Information about "best practices" of IRB operation and human subjects protection should be collected and shared among universities. Such best practices lists should be developed by the university community as well as by government agencies; the list of "Promising Practices" in the Appendix represents a starting point in the effort to develop such lists.

- d) NIH's recent policy change no longer to require IRB approval of grant applications prior to their peer review by NIH promises to reduce IRB workload with no loss of protections for human subjects. Campuses should determine how best to implement this policy as soon as feasible, consistent with their own circumstances.
- e) IRBs should ensure that their continuing protocol reviews are robust and promote a high degree of confidence in the protection of human subjects. While all protocols should be reviewed, particular attention should be paid to protocols involving more than minimal risk. Data Safety Monitoring Boards should share any analyses of adverse events with the IRBs and, as appropriate, with the NIH or the Office for Human Research Protections.
- f) Universities must educate faculty about existing federal and institutional policies regarding disclosure and management of real and perceived conflicts of interest, and impart to all university personnel the importance of assuring patients that financial interests will not affect proposed research protocols. Prior to submitting protocols for IRB review, investigators should provide any required financial interest disclosure to their designated institutional conflict of interest official or committee. Applications for IRB review should include reports from these officials or committees regarding any potential conflicts of interest, including financial ones, and their assessment of any potential impact on the proposed research.³ The IRB should take this information into account when deciding what information to include on informed consent forms about such conflicts, consistent with existing threshold-reporting requirements.

³Documents which explain the decisions by institutional conflict of interest committees or officials regarding whether and how these disclosed conflicts can be managed, reduced, or eliminated must be available for review by the IRB.

4. Increasing Resource Availability

Universities should provide the resources required to carry out the requirements of applicable laws and regulations, and to meet the highest ethical and professional standards, including the training of researchers and staff involved in human subjects research as well as IRB members. Research sponsors also should pay a fair share of the costs of systems of human subjects protections. Caps on recovery of administrative costs can limit the reimbursement of actual costs in some cases. Accordingly, alternative methods of direct or indirect cost recovery should be developed.

5. Ensuring Public Accountability by Increasing Information Available to the Public about University Systems Protecting Human Subjects

- a) To establish a reliable indicator of universities' acceptance of accountability for protecting human subjects, a reliable and robust oversight mechanism is required. The Task Force evaluated several possibilities, including: (i) the use of the institutional audits mentioned in Recommendation #1c; (ii) the use of campus self-reviews to see if an institution meets a set of "best practices" developed in Recommendation #3c, which would result in a sort of self-certification; and (iii) voluntary accreditation. The Task Force is clear that some additional public accountability mechanism is necessary, and recommends that universities pursue voluntary accreditation for conducting human subjects research. One model of voluntary accreditation is currently in effect for the use of animals in research. This is administered by the Association for Assessment and Accreditation of Laboratory Animal Care (AALAC). AALAC certifies institutions' animal research programs, conducts site visits every 3 years, and requires annual updates from accredited organizations,

which number 600 institutions in 11 countries.

The Public Responsibility in Medicine and Research (PRIM&R) group has recently formed the Association for Accreditation of Human Research Protections Programs (AAHRPP), which is beginning to develop draft performance standards and self-assessment tools for accreditation of human subjects research. The U.S. Department of Veterans Affairs has recently contracted with another group to accredit its human subjects activities. AAU institutions are urged to help support the establishment of effective accreditation programs, based on the principles recommended in this report, and voluntarily to seek accreditation of their human subjects research activities once such programs are established.

- b) The number of public members included on IRBs should be increased.
- c) There should be a forum for public airing of issues and views on protections of human subjects in research. One such forum is being established by HHS' new Office for Human Research Protections. The proposed advisory committee in that office will be a helpful focal point for discussion about how universities and other research performers can ensure that human subjects research protections meet the highest ethical standards.
- d) The university community should suggest that HHS (perhaps through the Office for Human Research Protections) develop a handbook of all federal rules and regulations, as well as specific departmental and agency contacts for questions that may arise during the IRB review of protocols. Such a handbook, which could also be on the Internet, would enhance IRB and institutional operations, and would help increase compliance with federal rules and regulations.

CONCLUSION AND CALL TO ACTION

The Task Force was animated by its concern that human subjects protections activities were not always achieving the highest standards. It encourages AAU members to assess promptly the status of their systems for protection of human subjects if they have not already done so. The Task Force believes that this report's recommendations provide a road map for improving these tremendously important protections systems, and urges campuses strongly to consider adopting these proposals as they move from an assessment of their systems to implementation of improvements. It is vitally important that human subjects research is done correctly as our universities continue to pursue scientific progress. As noted above, the use of human subjects in research is a privilege, not a right.

Today's ever-changing research environment requires continued vigilance to make sure that universities administer research as carefully as they conduct it. A final suggestion is to remain flexible in the future so as to adapt better to changes in research administration involving human subjects, to avoid encountering in the future the difficulties that the system faces today.

Finally, the partnership between research universities and

their principal research sponsor, the federal government, must be based on trust that universities are accountable for the research they perform. It is clear that if research universities do not move quickly to increase accountability for human subjects research, more prescriptive approaches may instead be pursued by either the executive or legislative branches of government - or both.

The Task Force therefore urges prompt attention to strengthen human subjects protections to:

- a) ensure that the highest standards are being followed in protecting the rights and welfare of human beings;
- b) ensure compliance with existing laws and regulations;
- c) ensure the integrity of the human subjects research;
- d) reduce the likelihood of inducing changes to laws and regulations that might bring other, unforeseen consequences; and
- e) bolster public confidence in human subjects research.

APPENDIX / PROMISING PRACTICES

One particularly important recommendation concerns information sharing of "best practices" among campuses, between campuses and government agencies, and by associations of institutions and research administrators (see recommendation #3c). In an effort to encourage that process, the Task Force has compiled a partial list of "Promising Practices" which were collected from some of the institutions participating in the Task Force, and which have been found effective in ensuring protections for human subjects. The Task Force hopes this sample list can serve as a catalyst for the more extensive best practices identification and sharing efforts that it recommends be initiated by NIH, FDA, the Association of American Medical Colleges (AAMC), Public Responsibility in Medicine and Research (PRIM&R), the Applied Research Ethical National Association (ARENA), and groups of universities.

The Promising Practices are more detailed than the Task Force recommendations, from which they are nevertheless logical extensions. Since each institution necessarily has different IRB processes, it is *not* the intent of the Task Force to recommend that this partial list of practices be adopted by all institutions, but rather that these Promising Practices be shared and discussed in the research community as part of the development, ultimately, of a list of best practices. Since each of these practices are descriptions by universities of how they do things, they are phrased as if a university representative were describing each particular promising practice to an audience. This helps to ensure that this list is used as a teaching aid, rather than as a required checklist—which it is not.

♦ Institutional Support

- We maintain regular communications with top management within the university.

♦ IRB Meetings/Membership Requirements

- We work to have enough IRBs to handle our protocol workload (some use 1 IRB per 250 open full board studies; others use 1 per 4/500 open full board studies).
- We hold regular IRB meetings (e.g., weekly or bi-weekly).
- We assign an alternate for each IRB member, which provides a dynamic committee makeup without overburdening members.
- We try to have an adequate budget (some use \$150-\$250K per IRB).

♦ Screening & Review of Applications

- We require the IRB staff to use a checklist to review all incoming applications before they are given to the IRB chair. If clear deficiencies are noted, the investigator addresses the deficiencies prior to IRB review. Applications sent to the full board are assigned a primary reviewer. The reviewer receives a copy of the full study protocol, grant application, and other relevant materials in addition to the materials sent to the full board (application, consent, advertisements, etc.) and a detailed checklist to assist in review.

♦ Continuing IRB Reviews

- For each IRB file, we establish a primary reviewer to examine the file and report to a subcommittee on the status of the clinical trial, which ensures that at least one IRB member is looking through the entire study file as a part of the continuing review.
- We hold subcommittee meetings to review the reports for continuation, which are open to all members and alternates, and to make recommendations for future action to the full IRB board. Prior to an IRB board meeting, we distribute the subcommittee recommendations and full continuation report to the board members for consideration and action at the next regularly

scheduled meeting. The board has an opportunity to discuss and vote on each individual continuation. All continuing data are carefully examined, but additional attention is provided to those studies involving more than minimal risk.

-We review some high-risk studies (e.g., involving new technology or a single investigator with unfunded studies) more frequently than annually and have developed criteria for determining which studies fall into which category.

♦ Written procedures

-We ensure that an up-to-date written procedural manual is available to investigators, and that forms and instructions used by IRB members meet current needs.

-We have prepared a set of written policies and procedures for addressing non-compliance.

-We have established an IRB newsletter and web page.

♦ Training Requirements

-We hold mandatory training classes and a follow-up assessment for IRB members, investigators, and their staff. We also hold monthly workshops on the basics of ethical and regulatory principles of human subjects research and monthly orientation meetings for all new faculty and staff.

-We have IRB chairs and vice chairs regularly attend national or regional IRB conferences, at the institution's expense. The office staff is also required to attend such meetings regularly. These activities are in addition to new member orientation, periodic administrative meetings of the IRB, and periodic mailings of educational materials.

♦ Managing Potential Conflict of Interest

-We include a series of questions regarding potential conflict of interest on the protocol review form used by investigators. If the investigator responds that a conflict of interest may exist, a committee reviews the

investigator's form. This review is in full accordance with both federal and institutional policies. The IRB takes into account the committee's analysis and report when deciding what will be included in the informed consent form or other appropriate protections.

♦ Vulnerable Populations

-We utilize consultants where there are concerns regarding the ability of a study participant to consent. This protects vulnerable populations in general, and cognitively impaired individuals in particular.

-We encourage investigators to take a conservative approach and obtain the additional signature of a relative or guardian (e.g., the legally authorized representative) whenever cognitive ability is in question.

♦ Institutional Audits

-All studies, irrespective of source of funding, are subject to an institutional audit process. The audit includes confirmation that:

- a) the protocol on file with the IRB is the protocol being used and that all modifications have been submitted to and approved by the IRB;
- b) the consent document being used is that which was approved by the IRB and the consents are appropriately signed and dated; and
- c) the investigator's adverse experience records match those reported to the IRB.

-Audit findings are reported to the IRB for review and appropriate action. A risk management group, which acts independently of the IRB and reports to a different institutional official, performs these audits.

-We select studies for audit at random with a goal of sampling sufficient files to measure effectiveness adequately (some perform audits on 50 studies each year).

♦ Strive for Continual Improvement

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